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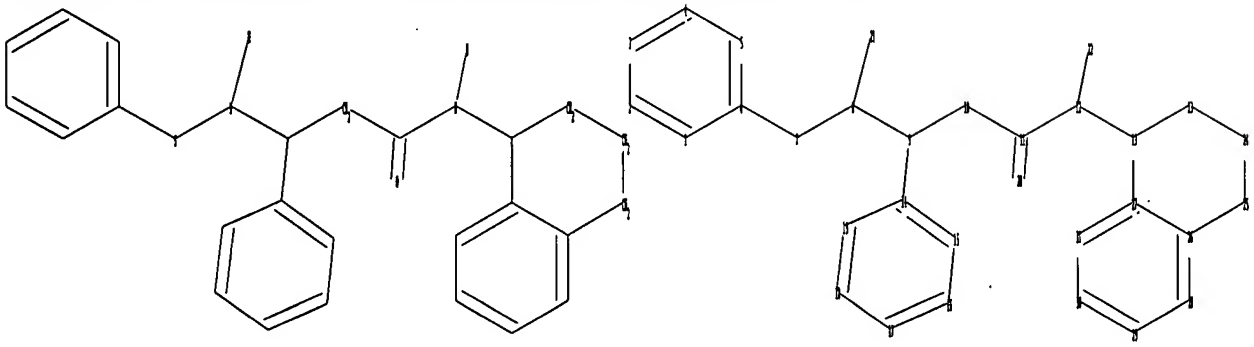
FILE 'HOME' ENTERED AT 12:58:22 ON 03 MAY 2007

=>
Uploading C:\Program Files\Stnexp\Queries\10823377.str

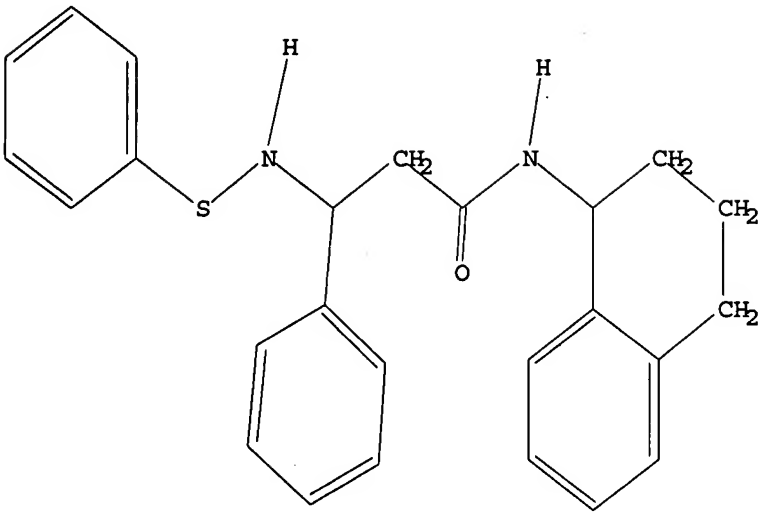


chain nodes :
7 8 9 10 11 12 20 21 22
ring nodes :
1 2 3 4 5 6 13 14 15 16 17 18 19 23 24 25 26 27 28 29 30 31
chain bonds :
6-7 7-8 8-9 8-21 9-10 9-14 10-11 11-12 11-20 12-13 12-22
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 13-23 13-27 14-15 14-19 15-16 16-17 17-18
18-19 23-24 24-25 25-26 26-27 26-28 27-31 28-29 29-30 30-31
exact/norm bonds :
6-7 7-8 8-9 11-12 11-20 12-13
exact bonds :
8-21 9-10 9-14 10-11 12-22 13-23 13-27 23-24 24-25 25-26
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 14-15 14-19 15-16 16-17 17-18 18-19 26-27
26-28 27-31 28-29 29-30 30-31
isolated ring systems :
containing 13 : 14 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:CLASS 21:CLASS 22:CLASS 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom
29:Atom 30:Atom 31:Atom

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

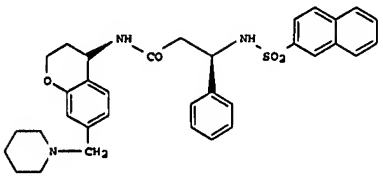
=> s l1 full
L3 192 SEA SSS FUL L1

=> file ca

=> s l3
L4 2 L3

=> d ibib abs fhitstr 1-2

L4 ANSWER 1 OF 2 CA COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 146:243251 CA
TITLE: Identification of a Nonpeptidic and Conformationally Restricted Bradykinin B1 Receptor Antagonist with Anti-Inflammatory Activity
AUTHOR(S): D'Amico, Derin C.; Aya, Toshi; Human, Jason; Potsch, Christopher; Chen, Jian Jeffrey; Biswas, Kaustav; Riahi, Bobby; Norman, Mark H.; Willoughby, Christopher A.; Hungate, Randall; Reider, Paul J.; Biddlecome, Gloria; Lester-Zeiner, Dianna; Van Staden, Carlo; Johnson, Eileen; Kamassah, Augustus; Arik, Leyla; Wang, Judy; Viswanadhan, Vellarkad N.; Groneberg, Robert D.; Zhan, James; Suzuki, Hideo; Toro, Andrea; Mareska, David A.; Clarke, David E.; Harvey, Darren M.; Burgess, Laurence E.; Laird, Ellen R.; Aakew, Benny; Ng, Gordon
CORPORATE SOURCE: Chemistry Research and Development, Neuroscience, HTS/Molecular Pharmacology, Molecular Structure and Design, and Inflammation, Amgen Inc., Thousand Oaks, CA, 91320, USA
SOURCE: Journal of Medicinal Chemistry (2007), 50(4), 607-610
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

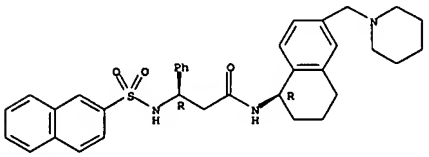


I

AB We report the discovery of chroman 28 (I), a potent and selective antagonist of human, nonhuman primate, rat, and rabbit bradykinin B1 receptors (0.4-17 nM). At 90 mg/kg s.c., 28 decreased plasma extravasation in two rodent models of inflammation. A novel method to calculate entropy is introduced and ascribed .apprx.30% of the gained affinity between "flexible" 4 (Ki = 132 nM) and "rigid" 28 (Ki = 0.77 nM) to decreased conformational entropy.
IT 784204-89-3P

L4 ANSWER 1 OF 2 CA COPYRIGHT 2007 ACS on STN (Continued)
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nonpeptidic antagonists of bradykinin B1 receptors)
RN 784204-89-3 CA
CN Benzenepropanamide, β-[(2-naphthalenylsulfonyl)amino]-N-[(1R)-1,2,3,4-tetrahydro-6-(1-piperidinylmethyl)-1-naphthalenyl]-, (βR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



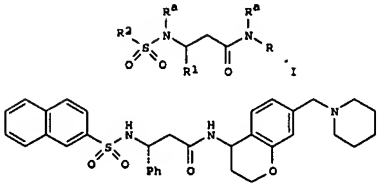
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CA COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 141:395300 CA
TITLE: Preparation of N-bicyclyl-3-[[(hetero)arylsulfonyl]amino]-3-(hetero)arylpropionamides as bradykinin receptor modulators for treatment of pain, inflammation, and other conditions
INVENTOR(S): Groneberg, Robert D.; Askew, Ben; D'Amico, Derin; Zhan, James; Toro, Andrea; Suzuki, Hideo; Mareska, David A.; Han, Nianh; Potsch, Christopher H.; Liu, Qinglan; Riahi, Babak; Yang, Kevin; Li, Aiwan; Yuan, Chester; Biswas, Kaustav; Harried, Scott; Nguyen, Tom; Qian, Wenyuan; Chen, Jian J.; Nomak, Rana
PATENT ASSIGNEE(S): Amgen, Inc., USA; Array Biopharma, Inc.
SOURCE: PCT Int. Appl., 375 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004092116	A1	20041028	WO 2004-US11105	20040412
WO 2004092116	A8	20050506		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004231070	A1	20041028	AU 2004-231070	20040412
CA 2521937	A1	20041028	CA 2004-2521937	20040412
US 2005124654	A1	20050609	US 2004-823377	20040412
EP 1631542	A1	20060308	EP 2004-759403	20040412
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2006522825	T	20061005	JP 2006-509895	20040412
PRIORITY APPLN. INFO.:			US 2003-461888P	P 20030410
			WO 2004-US11105	W 20040412

OTHER SOURCE(S): MARPAT 141:395300
GI

L4 ANSWER 2 OF 2 CA COPYRIGHT 2007 ACS on STN (Continued)

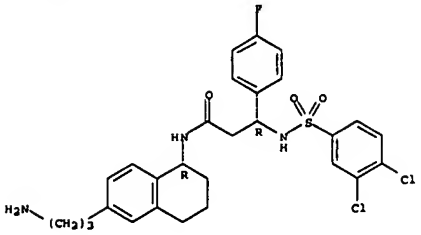


II

AB Title compds. I [wherein R = (un)substituted bicyclic carbocyclic or heterocyclic ring; R1 = (un)substituted cycloalkyl, aryl(alkyl), heteroaryl, heterocyclyl; R2 = (un)substituted aryl(alkenyl), heterocyclyl, heteroaryl; Ra = independently H, NH2COCH2, alkyl, (un)substituted aryl; and pharmaceutically acceptable derivs. thereof] were prepared as bradykinin receptor ligands. For example, N-(7-formylchroman-4-yl)-3-(naphth-2-ylsulfonylamino)-3-phenylpropionamide (7-step preparation given) was condensed with piperidine in the presence of NaBH(OAc)3 in N,N-dimethylacetamide and precipitated to give II·HCl. In a radioligand binding assay, the latter showed affinity for the human B1 and human B2 bradykinin receptors with Ki values of <100 nM and >1 μM, resp. Selected compds. of the invention are effective for treatment of pain and diseases, such as inflammation mediated diseases (no data).
IT 784205-21-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(bradykinin modulator; preparation of bicyclylpropionamides as bradykinin receptor modulators treatment of pain, inflammation, and other conditions)
RN 784205-21-6 CA
CN Benzenepropanamide, N-[(1R)-6-(3-aminopropyl)-1,2,3,4-tetrahydro-1-naphthalenyl]-β-[[(3,4-dichlorophenyl)sulfonyl]amino]-4-fluoro-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 2 OF 2 CA COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

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=> file marpat
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    10.47     182.78

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -1.46      -1.46

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FILE CONTENT: 1961-PRESENT VOL 146 ISS 18 (20070427/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US   2007060644 15 MAR 2007
DE 102006023116 15 MAR 2007
EP      1762248 14 MAR 2007
JP   2007059877 08 MAR 2007
WO   2007030662 15 MAR 2007
GB      2429975 14 MAR 2007
FR      2890657 16 MAR 2007
RU      2295953 27 MAR 2007
CA      2556850 24 FEB 2007

Expanded G-group definition display now available.

=> s l1 full
FULL SEARCH INITIATED 12:59:30 FILE 'MARPAT'
FULL SCREEN SEARCH COMPLETED -     8583 TO ITERATE

100.0% PROCESSED     8583 ITERATIONS  (     1 INCOMPLETE)        1 ANSWERS
SEARCH TIME: 00.00.07

L5            1 SEA SSS FUL L1

=> d ibib abs fqhit
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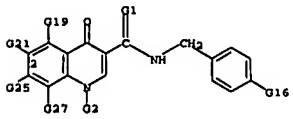
L5 ANSWER 1 OF 1 MARPAT COPYRIGHT 2007 ACS on STN
(ALL HITs ARE ITERATION INCOMPLETES)

ACCESSION NUMBER: 140:247064 MARPAT
TITLE: Method using quinolinecarboxamides and other heterocyclic compounds for preventing or treating atherosclerosis or restenosis
INVENTOR(S): Wathen, Michael W.; Wathen, Lynne K.
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 299 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004019932	A1	20040311	WO 2003-US26962	20030828
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003262947	A1	20040319	AU 2003-262947	20030828
US 2004186131	A1	20040923	US 2003-651309	20030828
PRIORITY APPLN. INFO.:			US 2002-407563P	20020830
			US 2003-467497P	20030502
			WO 2003-US26962	20030828

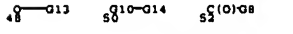
AB The invention provides a method for preventing or treating atherosclerosis or restenosis in mammals, which comprises administering an effective amount of a quinolinecarboxamide or other heterocyclic compound

MSTR 3 ITERATION INCOMPLETE

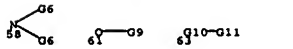


G1 = O / S
G2 = CH2CH2OH / 25 / 39 / heterocycle <containing 1-3 heteroatoms, 1 or more N, zero or more O, zero or more S (no other heteroatoms),

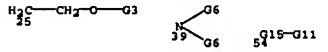
L5 ANSWER 1 OF 1 MARPAT COPYRIGHT 2007 ACS on STN (Continued)
1-7 C> (opt. substd. by OH)
G9 = alkyl <containing 1-7 C> (opt. substd. by OH) / heterocycle <containing 1-3 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 0 or more double bonds, mono- or bicyclic, 4-, 5-, 6- or 7-membered rings only> (opt. substd.) / aryl <containing 6 or more C, mono- or bicyclic> (opt. substd.)
G10 = S / S(O) / SO2
G11 = aryl <containing 6 or more C, mono- or bicyclic> (opt. substd.) / heterocycle <containing 1-3 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 0 or more double bonds, mono- or bicyclic, 4-, 5-, 6- or 7-membered rings only> (opt. substd.) / carbon chain <containing 1-7 C, 0 or more double bonds, 0 or more triple bonds> (opt. substd. by 1 or more G12)
G12 = OH / 48 / heterocycle <containing 1-3 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 0 or more double bonds, mono- or bicyclic, 4-, 5-, 6- or 7-membered rings only> (opt. substd.) / aryl <containing 6 or more C, mono- or bicyclic> (opt. substd.) / NH2 / alkylamino <containing 1-7 C> (opt. substd. by OH) / dialkylamino <each alkyl containing 1-7 C> (opt. substd. by OH) / CN / SH / 50 / F / Cl / Br / I / 52



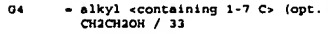
G13 = alkyl <containing 1-7 C> (opt. substd. by OH) / aryl <containing 6 or more C, mono- or bicyclic> (opt. substd.)
G14 = alkyl <containing 1-6 C> / aryl <containing 6 or more C, mono- or bicyclic> (opt. substd.)
G15 = O / S / S(O) / SO2
G16 = Cl / F / Br / CN / NO2
G17 = 58 / heterocycle <containing 1-3 heteroatoms, 1 or more N, zero or more O, zero or more S (no other heteroatoms), attached through 1 or more N, 0 or more double bonds, mono- or bicyclic, 4-, 5-, 6- or 7-membered rings only> (opt. substd.) / OH / 61 / CO2H / alkoxycarbonyl <containing 1-10 C> / heterocycle <containing 1-3 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 0 or more double bonds, mono- or bicyclic, 4-, 5-, 6- or 7-membered rings only> (opt. substd.) / aryl <containing 6 or more C, mono- or bicyclic> (opt. substd.) / CN / 63 / alkoxy <containing 2-4 C> (opt. substd.)



L5 ANSWER 1 OF 1 MARPAT COPYRIGHT 2007 ACS on STN (Continued)
attached through 1 or more N, 0 or more double bonds, mono- or bicyclic, 4-, 5-, 6- or 7-membered rings only> (opt. substd.) / 54 / heterocycle <containing 1-3 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), attached through 1 or more C, 0 or more double bonds, mono- or bicyclic, 4-, 5-, 6- or 7-membered rings only> (opt. substd.) / carbon chain <containing 1-7 C, 0 or more double bonds, 0 or more triple bonds> (opt. substd. by 1 or more G17) / carbocycle <containing 3-8 C, 0 or more double bonds, 0 or more triple bonds> (opt. substd. by G18) / Ph (opt. substd.)

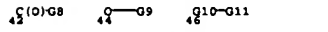


G3 = alkyl <containing 1-7 C> (opt. substd. by OH) / CH2CH2OH / 29



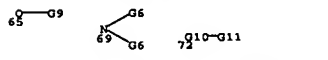
G4 = alkyl <containing 1-7 C> (opt. substd. by OH) / CH2CH2OH / 33

G5 = alkyl <containing 1-7 C> (opt. substd. by OH)
G6 = H / aryl <containing 6 or more C, mono- or bicyclic> (opt. substd.) / carbon chain <containing 1-7 C, 0 or more double bonds, 0 or more triple bonds> (opt. substd. by 1 or more G7)
G7 = NH2 / alkylamino <containing 1-7 C> (opt. substd. by OH) / dialkylamino <each alkyl containing 1-7 C> (opt. substd. by OH) / 42 / OH / 44 / CO2H / alkoxycarbonyl <containing 1-10 C> / heterocycle <containing 1-3 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 0 or more double bonds, mono- or bicyclic, 4-, 5-, 6- or 7-membered rings only> (opt. substd.) / aryl <containing 6 or more C, mono- or bicyclic> (opt. substd.) / CN / 46 / F / Cl / Br / I

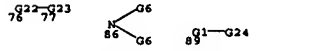


G8 = NH2 / alkylamino <containing 1-7 C> (opt. substd. by OH) / dialkylamino <each alkyl containing

L5 ANSWER 1 OF 1 MARPAT COPYRIGHT 2007 ACS on STN (Continued)
G18 = OH / 65 / CO2H / alkoxycarbonyl <containing 1-10 C> / heterocycle <containing 1-3 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 0 or more double bonds, mono- or bicyclic, 4-, 5-, 6- or 7-membered rings only> (opt. substd.) / aryl <containing 6 or more C, mono- or bicyclic> (opt. substd.) / CN / 69 / heterocycle <containing 1-3 heteroatoms, 1 or more N, zero or more O, zero or more S (no other heteroatoms), attached through 1 or more N, 0 or more double bonds, mono- or bicyclic, 4-, 5-, 6- or 7-membered rings only> (opt. substd.) / 72 / alkyl <containing 1-7 C> (opt. substd.)



G19 = H / F / Cl / Br / I / alkyl <containing 1-4 C> (opt. substd. by (1-3) G20)
G20 = F / Cl / Br / I
G21 = H / aryl <containing 6 or more C, mono- or bicyclic> (opt. substd.) / heterocycle <containing 1-3 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 0 or more double bonds, mono- or bicyclic, 4-, 5-, 6- or 7-membered rings only> (opt. substd.) / 76 / 86 / 89 / carbon chain <containing 1-8 C, 0 or more double bonds, 0 or more triple bonds> (opt. substd.)



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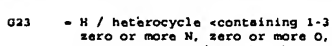
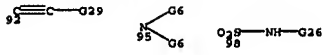
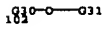


G23 = H / heterocycle <containing 1-3 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 0 or more double bonds, mono- or bicyclic, 4-, 5-, 6- or 7-membered rings only> (opt. substd.) / aryl <containing 6 or more C, mono- or bicyclic> (opt. substd.) / cycloalkyl <containing 3-8 C> / alkyl <containing 1-7 C> (opt. substd.)
G24 = alkyl <containing 2-7 C> (opt. substd. by OH)
G25 = H / F / Cl / Br / I / 92 / 95 / SO2NH2 / 98 / heterocycle <containing 1-3 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 0 or more double bonds, mono- or bicyclic, 4-, 5-, 6- or 7-membered rings only> (opt. substd.) / alkyl <containing 1-7 C> (opt. substd. by OH)

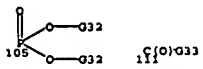
L5 ANSWER 1 OF 1 MARPAT COPYRIGHT 2007 ACS on STN (Continued)



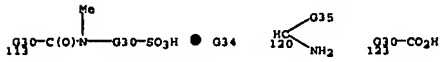
G26 = heterocycle <containing 1-3 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 0 or more double bonds, mono- or bicyclic, 4-, 5-, 6- or 7-membered rings only> (opt. substd.) / aryl <containing 6 or more C, mono- or bicyclic> (opt. substd.) / cycloalkyl <containing 3-8 C> / alkyl <containing 1-7 C> (opt. substd.)
G27 = H / F / Cl / Br / I / alkylthio <containing 1-7 C> / alkoxy <containing 1-7 C> (opt. substd. by 1 or more G28) / carbon chain <containing 1-7 C, 0 or more double bonds, 0 or more triple bonds> (opt. substd.)
G28 = F / Cl / Br / I / OH
G29 = heterocycle <containing 1-3 heteroatoms, zero or more N, zero or more O, zero or more S (no other heteroatoms), 0 or more double bonds, mono- or bicyclic, 4-, 5-, 6- or 7-membered rings only> (opt. substd.) / 102 / alkyl <containing 1-7 C> (opt. substd.)



G30 = (1-6) CH2
G31 = PO3H2 / 105 / 111



G32 = alkyl <containing 1-7 C>
G33 = 113 / 120 / aryl <containing 6 or more C, mono- or bicyclic> (opt. substd.) / alkyl <containing 1-6 C> (opt. substd. by G36) / 123



G34 = Na / K / Li
G35 = R <"amino acid side chain">
G36 = NH2 / alkylamino <containing 1-7 C> (opt. substd. by OH) / dialkylamino <each alkyl containing 1-7 C> (opt. substd. by OH)

L5 ANSWER 1 OF 1 MARPAT COPYRIGHT 2007 ACS on STN (Continued)
Derivative: or pharmaceutically acceptable salts
Patent location: claim 1

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

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=> d his

     (FILE 'HOME' ENTERED AT 12:58:22 ON 03 MAY 2007)

     FILE 'REGISTRY' ENTERED AT 12:58:33 ON 03 MAY 2007
L1              STRUCTURE UPLOADED
L2           11 S L1 SAM
L3          192 S L1 FULL

     FILE 'CA' ENTERED AT 12:59:03 ON 03 MAY 2007
L4            2 S L3

     FILE 'MARPAT' ENTERED AT 12:59:27 ON 03 MAY 2007
L5            1 S L1 FULL

=> file ca
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   126.48     309.26

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -0.73      -2.19

FILE 'CA' ENTERED AT 13:01:29 ON 03 MAY 2007
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FILE LAST UPDATED: 26 Apr 2007  (20070426/ED)

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  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s brandykinin
L6            1 BRANDYKININ

=> s bradykinin
L7        17906 BRADYKININ

=> s l7 and py<2004
      22728850 PY<2004
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L8        16177 L7 AND PY<2004

=> s l8 and (vitro and vivo)
         641233 VITRO
         431786 VIVO
L9          463 L8 AND (VITRO AND VIVO)

=> s l8 and (clinical stud?)
          81347 CLINICAL
        7962060 STUD?
           4827 CLINICAL STUD?
                  (CLINICAL(W)STUD?)
L10           3 L8 AND (CLINICAL STUD?)

=> d ibib abs 1-3
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L10 ANSWER 1 OF 3 CA COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 114:161845 CA
TITLE: Biochemical and clinical study of human liver prolyl endopeptidase
AUTHOR(S): Yoshioka, Nobuo
CORPORATE SOURCE: Med. Sch., Nagoya City Univ., Nagoya, 467, Japan
SOURCE: Nagoya-shiritsu Daigaku Igakkai Zasshi (1990), 41(3), 441-53
CODEN: NASDA6; ISSN: 0027-7606
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB To elucidate the physiol. role of prolyl endopeptidase (PEP) in liver, blood serum PEP activity in patients with various hepatic diseases was measured. In addition, PEP was isolated from human liver and its physicochem., immunochem., and enzymol properties were investigated. Serum PEP activity in patients with fulminant and chronic hepatitis was markedly increased compared to that in normal volunteers. A strong correlation was observed between serum PEP and γ-GTP in these patients. However, the activity in patients with acute hepatitis and cirrhosis was not increased. PEP was purified homogenously by SDS-PAGE. Its purifying magnification was 28,800-fold higher than that of the liver soluble fraction and its recovery percentage was 51%. The mol. weight of PEP was 72,000. It was stable at 40° or lower and pH 6.8-8.5 (optimum pH 6.5-6.7). From the results of study on the effects of various chemical substances on PEP activity, PEP is thought to be a serine protease. Anti-human hepatic PEP formed a homogenous sedimentation line against purified PEP from human liver extract fluid and human placenta extract fluid in double immunodiffusion. These sedimentation lines fused each other, suggesting that PEP is not organ specific. PEP cleaved proteins with mol. weight lower than 3,000 with proline-alanine bonds, but not proteins with mol. weight higher than 3,000. PEP decomposed angiotensin, oxytocin, and bradykinin, but not insulin or glucagon. These results suggest that PEP is probably useful as a new indicator of hepatic diseases.

L10 ANSWER 2 OF 3 CA COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 106:188950 CA
TITLE: Assessment of the analgesic effect of clofelin in cardiogenic pain (experimental and clinical study)
AUTHOR(S): Ignatov, Yu. D.; Mikhailovich, V. A.; Zaitsev, A. A.; Kuznetsova, O. Yu.; Panov, A. V.; Sinitsin, M. A.
CORPORATE SOURCE: I Leningr. Med. Inst., Leningrad, USSR
SOURCE: Farmakologiya i Toksikologiya (Moscow) (1987), 50(2), 36-9
CODEN: FATOAO; ISSN: 0014-8318
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Clofelin [4205-91-8] (0.1-0.25 mg/kg) depressed the emotional-behavioral manifestations evoked by introduction of bradykinin into the right atrium of the heart of the conscious rat. Unlike promedol (2-5 mg/kg), clofelin eliminated the pressor response to the exptl. angina. In humans during the acute period of myocardial infarction, clofelin taken orally (0.00015 g) decreased the emotional and motor manifestations associated with angina and stabilized central hemodynamics.

L10 ANSWER 3 OF 3 CA COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 81:116648 CA
TITLE: Experimental and clinical studies of renal arteriography with bradykinin
AUTHOR(S): Tsujita, Masaaki
CORPORATE SOURCE: Med. Sch., Osaka City Univ., Osaka, Japan
SOURCE: Osaka-shiritsu Daigaku Igaku Zasshi (1974), 23(1-3), 1-22
CODEN: OSDIAF; ISSN: 0472-1446
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Effects of bradykinin on renal arteriog. (RAG) were studied in exptl. animals and clin. cases. Exptl. studies were performed in pentobarbital anesthetized dogs; 10 μg of bradykinin was injected into the renal artery 1 min prior to RAG. In comparison, with usual RAG, bradykinin dilates the renal artery, shortened washout time, increased the d. of the nephrogram, enlarged longitudinal renal size, and decreased aortic reflux. Following RAG, renal function was transiently impaired, and recoverd completely 20 min after RAG. RAG with bradykinin also caused a transient impairment of renal function which was less than that in the usual RAG. In a clin. application of RAG with bradykinin, 15μg of bradykinin was administered into the renal artery 1 min prior to RAG. Findings similar to exptl. ones were observed Renal vasodilating effect of bradykinin was more effective in severely damaged kidneys as in severe hydronephrosis and in the terminal stage of renal tuberculosis. Accordingly, abnormalities of the kidney were more clearly demonstrated by RAG with bradykinin. There was no significant difference in renal function before and after clin. examination, and there was no persistent histol. damage in the kidney from RAG with bradykinin. Thus, RAG with bradykinin is useful for radiol. examination, especially of the kidney of patients with severely impaired hemodynamics.

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=> d his

     (FILE 'HOME' ENTERED AT 12:58:22 ON 03 MAY 2007)

     FILE 'REGISTRY' ENTERED AT 12:58:33 ON 03 MAY 2007
L1              STRUCTURE UPLOADED
L2           11 S L1 SAM
L3          192 S L1 FULL

     FILE 'CA' ENTERED AT 12:59:03 ON 03 MAY 2007
L4            2 S L3

     FILE 'MARPAT' ENTERED AT 12:59:27 ON 03 MAY 2007
L5            1 S L1 FULL

     FILE 'CA' ENTERED AT 13:01:29 ON 03 MAY 2007
L6            1 S BRANDYKININ
L7        17906 S BRADYKININ
L8        16177 S L7 AND PY<2004
L9          463 S L8 AND (VITRO AND VIVO)
L10           3 S L8 AND (CLINICAL STUD?)

=> s l9 not l10
L11         463 L9 NOT L10

=> s l11 and (inflamm? or pain or asthma)
        263920 INFLAMM?
         45508 PAIN
         33125 ASTHMA
L12         93 L11 AND (INFLAMM? OR PAIN OR ASTHMA)

=> d ibib abs 1-10
```

L12 ANSWER 1 OF 93 CA COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:175313 CA
TITLE: Structural modifications of highly potent bradykinin antagonists and their pharmacological consequences
AUTHOR(S): Stewart, John M.; Gera, Lajos; York, Eunice J.; Chan, Daniel C.; Bunn, Paul A., Jr.
CORPORATE SOURCE: Department of Biochemistry and Molecular Genetics, University of Colorado Medical School, Denver, CO, 80262, USA
SOURCE: Peptides 2000, Proceedings of the European Peptide Symposium, 26th, Montpellier, France, Sept. 10-15, 2000 (2001), Meeting Date 2000, 945-946. Editor(s): Martinez, Jean; Fehrentz, Jean-Alain. Editions EDK: Paris, Fr. CODEN: 69EDWK; ISBN: 2-84254-048-4
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Peptides and non-peptide bradykinin antagonists were synthesized, purified and characterized by standard methods. B-9430, which blocks both B2 and B1 receptors, is a truly outstanding antagonist. It is very potent, is totally resistant to enzymic degradation and is orally available. Use in this peptide of the new amino acid, α-(2-indanyl)glycine is important for conferring these remarkable properties. Higher potency was achieved with B-10206, which uses pentafluorophenylalanine and N-cycloheptylglycine. Potent and long-acting antagonists lacking the C-terminal Arg residue have been developed. Some of these are specific for B1 receptors (B-9958) or show combined B1-B2 antagonist activity (B-9858). The general desire for nonpeptide drugs has prompted the authors to develop small mol. BK antagonists. Among many compds., M-570 can be cited. While its anti-BK activity is not high, it has shown remarkable anticancer activity against small cell lung carcinoma (SCLC), both in vitro and in vivo. It is also active in vitro against prostate, colon, pancreas and breast cancer cell lines, as well as non-SCLC. The bradykinin antagonists stimulate apoptosis of cancer cells in vitro by a novel "biased agonist" mechanism; they stimulate one intracellular second-messenger pathway while inhibiting another. Taken together, these results strongly suggest that certain of these compds. should be developed as drugs for inflammation and cancers.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 93 CA COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:75913 CA
TITLE: Thrombin Activatable Fibrinolysis Inhibitor, a Potential Regulator of Vascular Inflammation
AUTHOR(S): Myles, Timothy; Nishimura, Toshihiko; Yun, Thomas H.; Nagashima, Mariko; Morser, John; Patterson, Andrew J.; Pearl, Ronald G.; Leung, Lawrence L. K.
CORPORATE SOURCE: Department of Med., Division of Hematology, Stanford University School of Medicine, Stanford, CA, 94305, USA
SOURCE: Journal of Biological Chemistry (2003), 278(51), 51059-51067 CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The latent plasma carboxypeptidase thrombin-activable fibrinolysis inhibitor (TAFI) is activated by thrombin/thrombomodulin on the endothelial cell surface, and functions in dampening fibrinolysis. In this study, the authors examined the effect of activated TAFI (TAFIa) in modulating the proinflammatory functions of bradykinin, complement C5a, and thrombin-cleaved osteopontin. Hydrolysis of bradykinin and C5a and thrombin-cleaved osteopontin peptides by TAFIa was as efficient as that of plasmin-cleaved fibrin peptides, indicating that these are also good substrates for TAFIa. Plasma carboxypeptidase N, generally regarded as the physiol. regulator of kinins, was much less efficient than TAFIa. TAFIa abrogated C5a-induced neutrophil activation in vitro. Jurkat cell adhesion to osteopontin was markedly enhanced by thrombin cleavage of osteopontin. This was abolished by TAFIa treatment due to the removal of the C-terminal Arg168 by TAFIa from the exposed SVVYGLR α4β1 integrin-binding site in thrombin-cleaved osteopontin. Thus, thrombin cleavage of osteopontin followed by TAFIa treatment may sequentially up- and down-modulate the pro-inflammatory properties of osteopontin. An engineered anticoagulant thrombin, E229K, was able to activate endogenous plasma TAFI in mice, and E229K thrombin infusion effectively blocked bradykinin-induced hypotension in wild-type, but not in TAFI-deficient, mice in vivo. The authors' data suggest that TAFIa may have a broad anti-inflammatory role, and its function is not restricted to fibrinolysis.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 93 CA COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 139:99221 CA
TITLE: Role of the bradykinin B2 receptor for the local and systemic inflammatory response that follows severe reperfusion injury
AUTHOR(S): Souza, Danielle G.; Pinho, Vanessa; Pesquero, Jorge L.; Lomez, Eliane S.; Poole, Steve; Juliano, Luiz; Correa, Ary, Jr.; Castro, M. Salete de A.; Teixeira, Mauro M.
CORPORATE SOURCE: Departamento de Bioquimica e Imunologia, Instituto de Ciencias Biologicas, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil
SOURCE: British Journal of Pharmacology (2003), 139(1), 129-139 CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 1 Bradykinin (BK) appears to play an important role in the development and maintenance of inflammation. Here, we assessed the role of the BK B2 receptor for the injuries that occur after ischemia and reperfusion (I/R) of the territory irrigated by the superior mesenteric artery. 2 Tissue (lung and duodenum) kallikrein activity increased after ischemia with greater enhancement after reperfusion. A selective inhibitor of tissue kallikrein, Phenylacetyl-Phe-Ser-Arg-N-(2,3-dinitrophenyl)-ethylenediamine (TKI, 0.001 - 10 mg ml-1), inhibited kallikrein activity in a concentration-dependent manner in vitro. In vivo, pretreatment with TKI (30 mg kg-1) prevented the extravasation of plasma and the recruitment of neutrophils. 3 Similarly, the bradykinin B2 receptor antagonists, HOE 140 (0.01 - 1.0 mg kg-1) or FR173657 (10.0 mg kg-1), inhibited reperfusion-induced increases in vascular permeability and the recruitment of neutrophils in the intestine and lungs. 4 In a model of more severe I/R injury, HOE 140 (1.0 mg kg-1) inhibited the increase in vascular permeability, neutrophil recruitment, hemorrhage and tissue pathol. Furthermore, HOE 140 significantly inhibited the elevations of TNF-α in tissue and serum and partially prevented lethality. This was associated with an increase in the concns. of IL-10 in tissue and serum. 5 Thus, our results demonstrate that, following intestinal I/R injury, there is an increase in tissue kallikrein activity and activation of BK B2 receptors. B2 receptor activation is essential for the development of inflammatory tissue injury and lethality. These results contrast with those of others showing that BK mostly exerts a protective role during I/R injury.
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 93 CA. COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 137:135201 CA
TITLE: Bradykinin-related compounds as new drugs for cancer and inflammation
AUTHOR(S): Stewart, John M.; Gera, Lajos; Chan, Daniel C.; Bunn, Paul A., Jr.; York, Eunice J.; Simkeviciene, Vitalija; Helfrich, Barbara
CORPORATE SOURCE: Department of Biochemistry, University of Colorado School of Medicine, Denver, CO, 80262, USA
SOURCE: Canadian Journal of Physiology and Pharmacology (2002), 80(4), 275-280 CODEN: CJPPA3; ISSN: 0008-4212
PUBLISHER: National Research Council of Canada
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bradykinin (BK) (Arg-Pro-Pro-Gly-Phe-Ser-Pro-Phe-Arg) is an important growth factor for small-cell lung cancer (SCLC) and prostate cancer (PC). These cancers have cells of neuroendocrine origin and express receptors for a variety of neuropeptides. BK receptors are expressed on almost all lung cancer cell lines and on many PC cells. The authors' very potent BK antagonist B9430 (D-Arg-Arg-Pro-Hyp-Gly-Igl-Ser-D-Igl-Oic-Arg) (Hyp, trans-4-hydroxy-L-proline; Igl, α-2-indanylglycine; Oic, octahydroindole-2-carboxylic acid) is a candidate anti-inflammatory drug but does not inhibit growth of SCLC or PC. When B9430 is dimerized by N-terminal crosslinking with a suberimide linker, the product B9870 is a potent growth inhibitor for SCLC both in vitro and in vivo in athymic nude mice. Daily i.p. injection at 5 mg/kg/day beginning on day 8 after SCLC SHP-77 cell implantation gave 65% inhibition of tumor growth. B9870 stimulates apoptosis in SCLC by a novel "biased agonist" action. The authors have also developed new small mimetic antagonists. BKM-570 (F5C-OC2Y-Atmp) (F5C, pentafluorocinnamic acid; OC2Y, O-2,6-dichlorobenzyl tyrosine; Atmp, 4-amino-2,2,6,6-tetramethylpiperidine) is very potent for inhibition of SHP-77 growth in nude mice. When injected daily i.p. at 5 mg/kg, M-570 gave 90% suppression of tumor growth. M-570 is more potent than the well-known anticancer drug cisPlatin (60% inhibition) or the recently developed SU5416 (40% inhibition) in this model. M-570 also showed activity against various other cancer cell lines in vitro (SCLC, non-SCLC, lung, prostate, colon, cervix) and inhibited growth of prostate cell line PC3 in nude mice. M-570 and related compds. evidently act in vivo through pathways other than BK receptors. These compds. have clin. potential for treatment of human lung and prostate cancers.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 93 CA COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 136:214233 CA
TITLE: Reciprocal regulation of endothelial substrate adhesion and barrier function
AUTHOR(S): Alexander, J. Steven; Zhu, Yanan; Elrod, John W.; Alexander, Brett; Coe, Laura; Kalogeris, T. J.; Fuseler, John
CORPORATE SOURCE: Department of Molecular and Cellular Physiology, Health Sciences Center, Louisiana State Univeraity, Shreveport, LA, 71130, USA
SOURCE: Microcirculation (New York, NY, United States) (2001), 8(6), 389-401
CODEN: MROCER; ISSN: 1073-9688
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To examine how cell-substrate adhesion is regulated during barrier changes produced by expoaure to inflammatory mediators. Lung microvascular endothelial monolayers were treated with test agents without/with blockers, and barrier was measured by transendothelial resistance; cell-substrate adhesion was assessed by surface area conservation after trypsin treatment of monolayers. Protein phosphorylation and distribution were assayed by immunoblotting and fluorescent microscopy, resp. H2O2, histamine, bradykinin, and thrombin, decreased endothelial barrier function, and enhanced adhesion to the substratum. H2O2 enhanced cell adhesion to the substrate in a concentration (0-1 mM)- and time (0-60 min)-dependent fashion. This effect of H2O2 reversed within 120 min of removal of H2O2 and was blocked by the mean arterial pressure (MAP) kinase inhibitor, PD98059 and by chelating cytoplasmic Ca2+ but not PKG or PKC inhibition. H2O2 also stimulated tyrosine phosphorylation of several proteins and increased the association of the focal adhesive proteins paxillin, talin, and vinculin with the cytoskeleton and may promote localization of these proteins to junctions. These data indicate that inflammatory mediators reduce cell-cell contact, contributing to reduced solute barrier and simultaneously enhanced substrate binding, which may be reciprocal events in barrier regulation in vitro and in vivo.
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 93 CA COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 136:132677 CA
TITLE: Regulation of leukocyte recruitment by polypeptidea derived from high molecular weight kininogen
AUTHOR(S): Chavakis, Triantafyllos; Kanse, Sandip M.; Pixley, Robin A.; May, Andreas E.; Isordia-Salas, Irma; Colman, Robert W.; Preissner, Klaus T.
CORPORATE SOURCE: Institute for Biochemistry, and Third Department of Internal Medicine, Justus-Liebig-Univ., Giessen, Germany
SOURCE: FASEB Journal (2001), 15(13), 2365-2376
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Proteolytic cleavage of single-chain, high mol. weight kininogen (HK) by kallikrein releases the short-lived vasodilator bradykinin and leaves behind a two-chain, high mol. weight kininogen (HKa) reported to bind to the β2-integrin Mac-1 (CR3, CD11b/CD18, αMβ2) on neutrophils and exert antiadhesive properties by binding to the urokinase receptor (uPAR) and vitronectin. The authors define the mol. mechanisms for the antiadhesive effects of HK related to disruption of β2-integrin-mediated cellular interactions in vitro and in vivo. In a purified system, HK and HKa inhibited the binding of soluble fibrinogen and ICAM-1 to immobilized Mac-1, but not the binding of ICAM-1 to immobilized LFA-1 (CD11a/CD18, αLβ2). This inhibitory effect could be attributed to HK domain 5 and to a lesser degree to HK domain 3, consistent with the requirement of both domains for binding to Mac-1. Accordingly, HK, HKa, and domain 5 inhibited the adhesion of Mac-1 but not LFA-1-transfected K562 human erythroleukemic cells to ICAM-1. Moreover, adhesion of human monocytic cells to fibrinogen and to human endothelial cells was blocked by HK, HKa, and domain 5. By using peptides derived from HK domain 5, the sequences including amino acids H475-G497 (and to a lesser extent, G440-H455) were identified as responsible for the antiadhesive effect, which was independent of uPAR. Finally, administration of domain 5 into mice, followed by induction of thioglycollate-provoked peritonitis, decreased the recruitment of neutrophils by ~70% in this model of acute inflammation. Taken together, HKa (and particularly domain 5) specifically interacts with Mac-1 but not with LFA-1, thereby blocking Mac-1-dependent leukocyte adhesion to fibrinogen and endothelial cells in vitro and in vivo and serving as a novel endogenous regulator of leukocyte recruitment into the inflamed tissue.
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 93 CA COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 136:112379 CA
TITLE: Oleanonic acid, a 3-oxotriterpene from Pistacia, inhibits leukotriene synthesis and has anti-inflammatory activity
AUTHOR(S): Giner-Larza, E. M.; Manez, S.; Recio, M. C.; Giner, R. M.; Prieto, J. M.; Cerda-Nicolas, M.; Rios, J. L.
CORPORATE SOURCE: Departament de Farmacologia, Universitat de Valencia, Facultat de Farmacia, Valencia, Burjassot, 46100, Spain
SOURCE: European Journal of Pharmacology (2001), 428(1), 137-143
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB One of the best known bioactive triterpenoids is oleanolic acid, a widespread 3-hydroxy-17-carboxy oleanane-type compound To determine whether further oxidation of carbon 3 affects anti-inflammatory activity in mice, different tests were carried out on oleanolic acid and its 3-oxo-analog oleanonic acid, which was obtained from Pistacia terebinthus galls. The last one showed activity on the ear edema induced by 12-deoxyphorbol-13-phenylacetate (DPP), the dermatitis induced by multiple applications of 12-O-tetradecanoyl-13-acetate (TPA) and the paw edemas induced by bradykinin and phospholipase A2. The production of leukotriene B4 from rat peritoneal leukocytes was reduced by oleanonic acid with an IC50 of 17 μM. Negligible differences were observed in the response of both triterpenes to DPP, bradykinin, and phospholipase A2, while oleanonic acid was more active on the dermatitis by TPA and on the in vitro leukotriene formation. In conclusion, the presence of a ketone at C-3 implies an increase in the inhibitory effects on models related to 5-lipoxygenase activity and on associated in vivo inflammatory processes.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 93 CA COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 136:15652 CA
TITLE: Effects of ANG II on bradykinin receptor gene expression in cardiomyocytes and vascular smooth muscle cells
AUTHOR(S): Kintsurashvili, Ekaterina; Duka, Irena; Gavras, Irene; Johns, Conrado; Farmakiotis, Dimitrios; Gavras, Haralambos
CORPORATE SOURCE: Hypertension and Atherosclerosis Section, Department of Medicine, Boston University School of Medicine, Boston, MA, 02118, USA
SOURCE: American Journal of Physiology (2001), 281(4, Pt. 2), H1778-H1783
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bradykinin has vasodilatory and tissue-protective effects exerted via its B2 type receptor, whereas the B1 receptor is constitutively absent but inducible by inflammation and toxins. In previous studies, the authors found that B2 receptor gene knockout mice exhibit overexpression of the B1 receptor, which assumes a vasodilatory function and is further upgraded in renovascular hypertension. The present study was designed to explore the effects of excess angiotensin II (ANG II) on B1 receptor and B2 receptor gene expression in mouse cardiomyocytes and rat vascular smooth muscle cells (VSMC) in vivo (after a 3-day infusion of 30 ng/min ANG II in 11 wild-type and in 13 genetically engineered mice with deleted B2 receptor gene) and in vitro (ANG II added in rat VSMC culture in the presence or absence of AT1 or AT2 receptor antagonist). Expression of B1 and B2 receptor mRNA was assessed by reverse transcriptase-polymerase chain reaction. ANG II infusion caused upregulation by 30% of the already significantly overexpressed B1 receptors in cardiomyocytes of the B2 receptor gene knockout mice, but in the wild-type mice it upregulated only the B2 receptor mRNA by 47%. The addition of ANG II in VSMC culture produced a time-dependent induction of B1 and upregulation of B2 receptor gene expression, maximal at 3 h (by fivefold), declining almost to baseline by 24 h. The addition of losartan completely blocked this effect, whereas the AT2 blocker PD-123319 made no difference, indicating that this is an AT1-mediated effect of ANG II. The data indicate that excess ANG II in subpressor doses in vivo upregulates expression of the B2 receptor, but in its absence, the already overexpressed B1 receptor is further upregulated, evidently assuming a counterregulatory response; in vitro, it transiently upregulates both bradykinin receptors.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 93 CA COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 136:1040 CA
TITLE: Proinflammatory characteristics of a nonpeptide bradykinin mimic, FR190997, in vivo
AUTHOR(S): Hayashi, Izumi; Ishihara, Keiko; Kumagai, Yuji; Majima, Masataka
CORPORATE SOURCE: Department of Pharmacology, Kitasato University School of Medicine, Sagamihara, 228-8555, Japan
SOURCE: British Journal of Pharmacology (2001), 133(8), 1296-1306
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Proinflammatory potency of the nonpeptide bradykinin (BK) B2 receptor agonist FR190997 (8-[2,6-dichloro-3-[N-[(E)-4-(N-methylcarbamoyl)cinnamidoacetyl]-N-methylamino]benzyloxy]-2-methyl-4-(2-pyridylmethoxy)quinoline) was investigated. Intradermal injection of FR190997 (0.03-3 nmol site-1) into dorsal skin of rats increased vascular permeability in a dose-dependent manner. The effect was less than that of BK, but it was long-acting and was inhibited by treatment with FR173657 (3 mg kg-1, p.o.). Captopril (10 mg kg-1, i.p.) did not enhance the plasma extravasation by FR190997 (0.3 nmol site-1) in the presence of soybean trypsin inhibitor (SBTI, 30 μg site-1). S.c. injection of FR190997 (3 nmol site-1) into the hindpaw of mice markedly induced paw swelling. The edema lasted up to 3 h after the injection. Administration of indomethacin or NS-398 (10 mg kg-1, i.p.) significantly reduced it at 3 h after the injection. Simultaneous i.p. injection of prostaglandin (PG) E2 (1 nmol site-1) or beraprost sodium (0.5 nmol site-1) with FR190997 (5 nmol site-1) greatly enhanced frequency of writhing reactions in mice. FR190997 (0.3-30 nmol kg-1, i.v.) showed less increase in airway opening pressure (Pao) in the guinea-pig after i.v. injection. Furthermore, FR190997 (0.03-30 nmol) resulted in a very weak contraction of tracheal ring strips and lung parenchymal sections in vitro. In mice sponge implants, topical application of FR190997 increased angiogenesis and granulation with enhanced expressions of basic fibroblast growth factor (bFGF) and vascular endothelial growth factor (VEGF) mRNAs. These results indicate that FR190997 has proinflammatory long-lasting characteristics and it might be "a stable tool" for studying the role of BK B2 receptor in vivo.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 93 CA COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 135:3934 CA
TITLE: Endothelial kinin B1-receptors are induced by myocardial ischaemia-reperfusion in the rabbit
AUTHOR(S): Mazenot, C.; Loufrani, L.; Henrion, D.; Ribuout, C.; Muller-Esterl, W.; Godin-Ribuot, D.
CORPORATE SOURCE: LSCPA, UFR Pharm., Universite Grenoble I, Fr.
SOURCE: Journal of Physiology (Cambridge, United Kingdom) (2001), 530(1), 69-78
CODEN: JPHYA7; ISSN: 0022-3751
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Kinin B1-receptors are induced by various inflammatory stimuli. Since myocardial ischemia-reperfusion results in inflammation, we questioned whether it could induce B1-receptor-dependent responses to des-Arg9-bradykinin (DBK). Thirty-six rabbits were submitted either to a 30 min coronary occlusion followed by a 3 h reperfusion or to a sham operation. The response to DBK was then tested in vivo on mean arterial pressure (MAP) and in vitro on isolated hearts and arterial rings. DBK induced a dose-dependent decrease in MAP in the ischemia-reperfusion group (DBK, 10 μg kg-1, intra-arterial: -12 ± 2 vs. -5 ± 2 mmHg in the sham group, P < 0.02), which was significantly antagonized by [Leu8]-des-Arg9-bradykinin (LBK), a B1-receptor antagonist. Following ischemia-reperfusion, isolated hearts responded to DBK by a decrease in coronary perfusion pressure greater than that of the sham group. DBK dose-dependently decreased the isometric force of isolated carotid rings (DBK, 10-5 M: -9 ± 2 vs. -1 ± 2% in the sham group, P < 0.02) and mesenteric arteries (DBK, 10-6 M: -38 ± 7% vs. -3 ± 2% in the sham group, P < 0.001). The vascular effects of DBK seen after ischemia-reperfusion were significantly antagonized by LBK. The presence of B1-receptors in ischemia-reperfusion animals was confirmed by immunolocalization and Western blot anal. This study demonstrates that myocardial ischemia-reperfusion induces a global induction of functional kinin B1-receptors in the endothelium.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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---Logging off of STN---

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Executing the logoff script...

=> LOG Y

STN INTERNATIONAL LOGOFF AT 13:08:35 ON 03 MAY 2007